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30623	7590	07/07/2010	EXAMINER	
MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C			HUMPHREY, LOUISE WANG ZHIYING	
ONE FINANCIAL CENTER			ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/664,610	Applicant(s) WILSON ET AL.	
	Examiner LOUISE HUMPHREY	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 April 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 127-137 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 127-137 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/16/2010</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is in response to the amendment filed 09 April 2010.

Claims 1-126 have been cancelled.

Claims 127-137 are pending and currently examined.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 16 April 2010 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. See attached signed and dated copy of form 1449/PTO.

Specification

The abstract of the disclosure is objected to because it does not pertain to the claimed invention. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Art Unit: 1648

Where applicable, the abstract should include the following:

- (1) if a machine or apparatus, its organization and operation;
- (2) if an article, its method of making;
- (3) if a chemical compound, its identity and use;
- (4) if a mixture, its ingredients;
- (5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: a method for identifying an aptamer regulator.

The use of the trademark SELEX has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. The generic terminology of “*in vitro* aptamer selection process” as recited in the brief description of Figure 1 ([0019]), should accompany the “SELEXTM” wherever it appears in the specification.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

Art Unit: 1648

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

(Prior Rejection – Withdrawn) The rejection of claims 127-133, 136 and 137 under 35 U.S.C. §103(a) as being unpatentable over Cubicciotti *et al.* (US 6,287,765 B1) is withdrawn.

(Prior Rejection – Withdrawn) The rejection of claims 135 under 35 U.S.C. §103(a) as being unpatentable over Cubicciotti *et al.* (US 6,287,765 B1) in view of Gallivan *et al.* (US 2003/0064931 A1, effectively filed 28 September 2001) is withdrawn.

(Prior Rejection – Withdrawn) The rejection of claims 134 under 35 U.S.C. §103(a) as being unpatentable over Cubicciotti *et al.* (US 6,287,765 B1) in view of Gold *et al.* (US 5,763,173, patented 9 June 1998, No. A28 in IDS 22 May 2006) is withdrawn.

Response to Arguments

Applicant's arguments, see page 7-14, filed 09 April 2010, with respect to the rejections of claims 127-137 under 35 U.S.C. §103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new grounds of rejection are made in view of the newly found prior art references.

NEW REJECTIONS

Claims 127-130, 136 and 137 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lupold *et al.* (US 6,933,114 B2, filed 16 October 2001).

The instant claims are directed to a method for identifying an aptamer regulator comprising:

(a) providing a target and a target partner that do not bind to each other in the absence of an aptamer regulator;

(b) contacting a mixture of nucleic acids with the target and the target partner under conditions that disfavor efficient binding between the target and the target partner;

(b) partitioning nucleic acids bound to a target-target partner (T/TP) complex from unbound nucleic acids; and

(c) retaining the nucleic acids bound to the T/TP complex, thereby identifying an aptamer that binds to a target, wherein binding of the aptamer to the target increases the binding affinity of the target for the target partner relative to when the target is not bound by the aptamer regulator.

The claim limitation of binding between a "target" and "target partner" reads on any interaction between a target and another molecule. The claim limitation of "aptamer regulator" reads on a nucleic acid ligand.

Claims 128 and 129 further limit the mixture of nucleic acids to a target-specific and diversified pool. Claim 130 further limits the target partner to be immobilized. Claim 136 further comprises the step of amplifying the retained nucleic acids and repeating steps a) to d). Claim 137 further comprises the step of screening the retained nucleic acids for a desired functional activity.

Art Unit: 1648

Lupold *et al.* discloses a basic method for identifying an aptamer comprising the steps of contacting a mixture of nucleic acids with the target, partitioning nucleic acids bound to target from the unbound nucleic acids, amplifying the retained nucleic acids (col. 8, lines 3-13), and repeating the partitioning/amplifying steps (col. 10, lines 22-52). The candidate mixture is a mixture of nucleic acids of differing sequences with fixed sequences surrounding a randomized region (col. 10, lines 8-21). The fixed sequences can mimic a sequence known to bind to the target (col. 10, line 13-14), which renders the mixture of nucleic acids target-specific. Such randomized sequences are known in the art to render a diversified pool of nucleic acids as Lupold *et al.* also discloses the diversity of the structures employed by an aptamer library (col. 4, lines 43-44). Lupold *et al.* further discloses the step of screening the retained or identified nucleic acids for a desired functional activity such as the ability to inhibit NAALADase enzyme activity (col. 15, lines 63-64).

Lupold *et al.* does not explicitly disclose a target partner and the desired functional activity of the aptamer binding to the target to increase the binding affinity of the target for the target partner relative to the unbound target.

However, Lupold *et al.* suggests that the basic aptamer selection method has been modified to achieve specific objectives (col. 10, lines 53-54) and further explicitly suggests nucleic acid ligands, often referred to as “aptamers,” having desirable functions on a target including binding of the target, catalytically changing the target, reacting with the target in a way which modifies/alters the target or the functional activity of the target, facilitating the reaction between the target and another molecule (col. 7,

Art Unit: 1648

lines 53-61), which means the same as the claim limitation of “an aptamer regulator that binds to a target wherein the binding increases the binding affinity of the target for the target partner relative to the affinity of the target for the target partner when the target is not bound by the aptamer regulator” in the instant claims.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Lupold *et al.* so as to further include, in each method step, a target partner that does not bind the target without an agonist like the aptamer regulator. One having ordinary skill in the art would have been motivated to make such a modification to select for aptamers with the desirable functions of binding of the target, catalytically changing the target, reacting with the target in a way which modifies/alters the target or the functional activity of the target, and facilitating the reaction between the target and another molecule, as per the suggestion of Lupold *et al.*

Although Lupold *et al.* does not disclose immobilizing a target partner, Lupold *et al.* discloses immobilizing the target on a solid support (col. 8, lines 62-67 continued on to col. 9, line 6). It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Lupold *et al.* so as to immobilize the target partner rather than the target. One having ordinary skill in the art would have been motivated to make such a modification for the convenience of partitioning nucleic acid-bound target that is bound to the target partner.

There would have been a reasonable expectation of success, given the variety of modifications to the basic method that are routinely practiced by one of ordinary skill in the art, as disclosed by Lupold *et al.* (col. 10, lines 53 to col. 11, line 54). Thus, the

invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 131-133 and 135 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lupold *et al.* (US 6,933,114 B2, filed 16 October 2001) in view of Geiger *et al.* (1996, IDS 16 April 2010).

The instant invention further comprises: (1) a negative selection prior to step (a) comprising partitioning and discarding nucleic acids bound to the target partner; and (2) the step of removing the retained nucleic acids from the target-target partner (T/TP) complex by eluting the nucleic acids with free excess target.

The disclosure of Lupold *et al.* is set forth above. Lupold *et al.* does not disclose the prior step of negative selection or the step of eluting the nucleic acids with excess free target.

Geiger *et al.* discloses the step (1) of a negative selection with a non-desired target in which the pool of nucleic acids are partitioned and washed away with a non-desired target, citrulline, prior to the selection of arginine-specific aptamers; and the step (2) of elution of arginine-specific aptamers with an excess of free target, a 20 mM solution of arginine (page 1030, right column, see the passage entitled "Selections").

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the selection method disclosed by Lupold *et al.* so as to further include the step of negative selection with a non-desired target, such as the target partner in the instant case, and the step of eluting the nucleic acids with free

Art Unit: 1648

excess target, as suggested by Geiger *et al.*, with a reasonable expectation of success because this selection scheme and this elution technique are routine optimizations known in the art of aptamer selection. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 133 and 134 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lupold *et al.* (US 6,933,114 B2, filed 16 October 2001) in view of Firer *et al.* (30 October 2001).

The instant invention further comprises the step of removing the retained nucleic acids from the T/TP complex by eluting with an agonist competitor to the target.

The disclosure of Lupold *et al.* is set forth above. Lupold *et al.* does not disclose eluting the nucleic acids with an agonist competitor to the target.

Firer *et al.* discloses the strategy of competitive elution with excess ligands from a target molecule immobilized to a resin in a chromatography column (page 438, third complete paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the selection method disclosed by Lupold *et al.* so as to further include the step of eluting the nucleic acids with an agonist competitor to displace the nucleic acid ligands bound to the target, as suggested by Firer *et al.*, with a reasonable expectation of success because competitive elution, an elution technique using a competitor for the same binding site on the target to remove the bound ligand, is a routine procedure that has been demonstrated in the art to separate the ligand from

Art Unit: 1648

the target protein, as disclosed in Firer *et al.* Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Application/Control Number: 10/664,610
Art Unit: 1648

Page 11

/Louise Humphrey/
Examiner, Art Unit 1648